Claims:

1. A method for identifying a compound capable of promoting deactivation of a membrane bound active small GTPase, comprising:

incubating in the presence of a test compound a live cell expressing the membrane bound small GTPase and having a small GTPase specific reporter thereof, and,

monitoring association of the reporter with the membrane bound small GTPase,

wherein a change in association of the reporter with the membrane bound small GTPase is indicative that the test compound is capable of promoting deactivation of the membrane bound active small GTPase.

2. A method for identifying a compound capable of enhancing the intrinsic GTPase activity of an membrane bound active small GTPase, and thereby promoting deactivation of the membrane bound small GTPase, comprising:

incubating in the presence of a test compound a live cell expressing the membrane bound small GTPase and having a small GTPase specific reporter thereof, and,

monitoring association of the reporter with the membrane bound small GTPase,

wherein a change in association of the reporter with the membrane bound small GTPase is indicative that the test compound is capable of enhancing the intrinsic GTPase activity of the membrane bound active small GTPase.

3. A method for identifying a compound capable of inhibiting activation of a membrane bound small GTPase, comprising:

incubating in the presence of a test compound a live cell expressing the membrane bound small GTPase and having a small GTPase specific reporter thereof, and,

monitoring association of the reporter with the membrane bound small GTPase,

wherein a change in the association of the reporter with the membrane bound small GTPase is indicative that the test compound is capable of inhibiting activation of the membrane bound small GTPase.

4. A method for identifying a compound capable of inhibiting GTP loading on a membrane bound small GTPase, comprising:

incubating in the presence of a test compound a live cell expressing the small GTPase and a small GTPase specific reporter thereof and optionally overexpressing a GEF that activates the membrane bound small GTPase, and,

monitoring association of the reporter with the membrane bound small GTPase,

wherein a change in the association of the reporter with the membrane bound small GTPase is indicative that the test compound is capable of inhibiting GTP loading.

5. A method for identifying a compound capable of inhibiting GTP loading on a membrane bound small GTPase by directly blocking guanine nucleotide exchange factor-stimulated GDP/GTP exchange, or by inhibiting upstream pathways that lead to the activation of the exchange factor, comprising:

incubating in the presence of a test compound a live cell expressing the membrane bound small GTPase and having a small GTPase specific reporter thereof and optionally overexpressing a GEF that activates the membrane bound small GTPase, and,

monitoring association of the reporter with the membrane bound small GTPase,

wherein a change in the association of the reporter with the membrane bound small GTPase is indicative that the test compound is capable of inhibiting GTP loading.

6. A method for identifying a compound capable of modulating interaction of a membrane bound small GTPase with a binding partner, comprising:

incubating in the presence of a test compound a live cell expressing the membrane bound small GTPase and having a small GTPase specific reporter thereof, and,

monitoring association of the reporter with the membrane bound small GTPase,

wherein a change in association of the reporter with the membrane bound small GTPase is indicative that the test compound is capable of modulating the interaction between the membrane bound small GTPase and its binding partner.

7. A method according to claim 6 wherein the binding partner is an effector of the small GTPase or comprises a peptide derived from the effector, optionally linked to a detectable marker.

8. A method according to claim 6 wherein the binding partner is the reporter specific for the membrane bound small GTPase.

9. A method according to any preceding claim wherein the small GTPase is bound at one or more of the following membranes: the plasma membrane, Golgi apparatus membrane, endomembrane, mitochondrial membrane, outer nuclear membrane, inner nuclear membrane, endoplasmic reticulum, sarcoplasmic reticulum and/or a membrane of transport and/or secretory vesicles.

10. A method according to any of the preceding claims wherein the membrane bound small GTPase is a Ras superfamily GTPase.

11. A method according to any of the preceding claims wherein the membrane bound small GTPase is a Ras, Rho, Ran, Arf/Sar1, or Rab/YPT1 subfamily GTPase.

12. A method according to any of the preceding claims wherein the membrane bound small GTPase is one or more Ras GTPase selected from the group comprising H-Ras, K-Ras and N-Ras.

13. A method according to any of the preceding claims, wherein the association of the reporter with an active membrane bound small GTPase is monitored.

14. A method according to any of the preceding claims wherein the small GTPase is a hyperactive or a constitutively active mutant small GTPase.

15. A method according to claim 12 or claim 13, wherein the small GTPase is Ras.

16. A method according to claim 12, wherein the small GTPase is hyperactive or oncogenic Ras.

17. A method according to any preceding claim wherein the reporter is an active membrane bound small GTPase specific reporter.

18. A method according to claim 17, wherein the change in association of the reporter with the membrane is dissociation of the reporter from the membrane

19. A method according to any of claims 1 to 16, wherein the reporter is an inactive membrane bound small GTPase specific reporter.

20. A method according to any preceding claim, wherein the reporter comprises a small GTPase specific binding moiety and a detectable marker moiety.

21. A method according to claim 20, wherein the small GTPase specific binding moiety is a peptide derived from an effector of the small GTPase.

22 A method according to claim 21, wherein the small GTPase specific binding moiety is a peptide derived from an effector of the small GTPase having one or more point mutations that increase the affinity of the peptide for the small GTPase relative to the affinity of the wild type effector for the small GTPase.

23. A method according to any of claims 20 to 22, wherein the small GTPase is a Ras and the small GTPase-specific binding moiety is an active-Ras-specific-binding moiety.

24. A method according to claim 23, wherein the active-Ras specific binding moiety is Raf-1-RBD, or a derivative thereof.

25. A method according to any of claims 20 to 22, wherein the small GTPase is Cdc42 and the small GTPase specific binding moiety is an active Cdc42 specific binding moiety.

26. A method according claim 25, wherein the active Cdc42 specific binding moiety is WASP-CRIB, or a derivative thereof.

27. A method according to any one of claims 20 to 22, wherein the small GTPase monitored is Rac and the small GTPase specific binding moiety is an active Rac specific binding moiety.

28. A method according to claim 27, wherein the active Rac specific binding moiety is the CRIB domain from P21 activated kinase, or a derivative thereof.

29. A method according to any of claims 20 to 22, wherein the small GTPase is Rap1 and the small GTPase specific binding moiety is an active Rap1 specific binding moiety.

30. A method according claim 29, wherein the active Rap1 specific binding moiety is a peptide derived from RalGDS, or a derivative thereof.

31. A method according to any of the preceding claims, wherein the reporter is a reporter protein.

32. A method according to claim 31, wherein the reporter is expressed within the cell.

33. A method according to claim 31, wherein the reporter is introduced into the cell.

34. A method according to any of claims 20 to 33, wherein the detectable marker moiety is a luminescent protein.

35 A method according to any of claims 20 to 33, wherein the detectable marker moiety is a fluorescent protein.

36. A method according to claim 35, wherein the fluorescent protein is a red, orange yellow, yellow-green, green-yellow, green, blue, cyan, fluorescent protein.

37. A method according to claim 35 or claim 36, wherein the fluorescent protein is a wild type, enhanced, destabilised enhanced or red-shift or folding mutant fluorescent protein.

38. A method according to any one of claims 35 to 37, wherein the fluorescent protein is monomeric.

39. A method according to any one of claims 35 to 38 wherein a FRET method using two fluorescent proteins is used to monitor location of the reporter within the cell.

40. A method according to claim 39, wherein FRET is between a plasma membrane localised fluorophore and a membrane bound small GTPase specific fluorescent reporter.

41. A method according to any one of claims 20 to 30, wherein the small GTPase specific protein moiety is expressed within the cell and labelled *in vivo* with a fluorescent marker.

42. A method according to any one of claims 20 to 30, wherein the small GTPase specific protein moiety is introduced into the cell and labelled *in vivo* with a fluorescent marker.

43. A method according to any one of claims 20 to 30, wherein a membrane bound small GTPase specific protein moiety labelled with a fluorescent marker is introduced into the cell.

44. A method according to any of claims 35 to 43, wherein monitoring is performed by fluorescence microscopy.

45. A method according to claim 44, wherein the fluorescence microscopy is performed by wide-field or total internal reflection fluorescence microscopy or fluorescence lifetime imaging or confocal imaging.

46. A method according to any of the preceding claims, wherein the cell is a tumour cell

47. A method according to any of the preceding claims wherein the cell is a primary tumour cell.

48. A method according to any of claims 1 to 46 wherein the cell is from an *in vitro* model cell line.

49. A method according to claim 39 wherein the cell is a Cho, Cos, Jurkat-T or HeLa cell.

50. A method for identifying a compound capable of promoting deactivation of a membrane bound active Ras, comprising:

incubating in the presence of a test compound a live cell expressing Ras and a specific reporter thereof, preferably GFP-RBD or a derivative thereof, and,

monitoring association of the reporter, preferably GFP-RBD or a derivative thereof, with the membrane bound active Ras,

wherein a dissociation of the reporter from the membrane bound active Ras is indicative that the test compound is capable of promoting deactivation of the membrane bound active Ras.

51. A method according to any of the preceding claims performed in high throughput format.

52. An assay for a small GTPase antagonist compound comprising a method of any of the preceding claims.

53. A high throughput assay for a small GTPase antagonist compound comprising a method of any of the preceding claims.

54. A high throughput screening method for identifying a compound capable of promoting deactivation of a membrane bound active Ras, comprising:

incubating in the presence of a test compound a live cell expressing Ras and a specific reporter thereof, preferably GFP-RBD or a derivative thereof, and,

monitoring association of the reporter, preferably GFP-RBD or a derivative thereof, with the membrane bound active Ras,

wherein a dissociation of the reporter from the membrane bound active Ras is indicative that the test compound is capable of promoting deactivation of the membrane bound active Ras.

55. A compound identifiable or identified by a method or assay of any of the preceding claims.

56. The use of a compound of claim 55 as a medicament.

57. The use of a compound of claim 55 in the manufacture of a medicament for the treatment of the human or animal body.

58. The use of a compound of claim 55 in the manufacture of a medicament for the treatment of tumours.

59. The use of a compound of claim 55 in the manufacture of a medicament for the treatment of cancer.